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Heart rate variability biofeedback in chronic disease management: A systematic review

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ABSTRACT

Background: Heart rate variability biofeedback (HRVB) is a non-pharmacological intervention used in the management of chronic diseases.
Method: A systematic search was performed according to eligibility criteria including adult chronic patients, HRVB as main treatment with or without control conditions, and psychophysiological outcomes as dependent variables.
Results: In total, 29 articles were included. Reported results showed the feasibility of HRVB in chronic patients without adverse effects. Significant positive effects were found in various patient profiles on hypertension and cardiovascular prognosis, inflammatory state, asthma disorders, depression and anxiety, sleep disturbances, cognitive performance and pain, which could be associated with improved quality of life. Improvements in clinical outcomes co-occurred with improvements in heart rate variability, suggesting possible regulatory effect of HRVB on autonomic function.
Conclusions: HRVB could be effective in managing patients with chronic diseases. Further investigations are required to confirm these results and recommend the most effective method.

1. Introduction

The World Health Organization considers that noncommunicable chronic diseases, including cardiovascular disease, cancer, chronic respiratory disease, diabetes and mental health conditions, were responsible for almost 70 % of all deaths worldwide in 2016.[1] Their global prevalence is increasing and this burden is leading to growing social and economic consequences.[2] The quality and effectiveness of disease management is therefore a major concern for improving patient care and reducing health care costs.[3] Chronic diseases are generally related to impairments of the autonomous nervous system (ANS) balance resulting in sympathetic overstimulation and a lack of vagal activity.[4] This dysautonomia could be considered as a consequence of illness but also as a major risk factor involved in the starting point of chronic diseases and in their evolution. Disease state implies several physiological alterations such as hypersecretion of stress hormones (e.g., cortisol, norepinephrine), sleep alterations, release of inflammatory mediators (e.g., IL-6), hypertension, or immune dysfunction, which may contribute to health deterioration and the development of comorbidities.[5] Moreover, a model based on several epidemiological studies established a link between the aetiopathogenesis of cardiovascular diseases, cancer and Alzheimer's disease with low vagus nerve activity.[6] Against this background, recent research has focused on interventions that can increase vagal activity and restore autonomous balance.

Heart rate variability (HRV), measured at rest, is used to index the autonomic function and is considered as a biomarker of health.[7] High

Abbreviations: HRV, heart rate variability; ECG, electrocardiogram; ANS, autonomic nervous system; SNS, systematic nervous system; PNS, parasympathetic nervous system; BP, blood pressure; RSA, respiratory sinus arrhythmia; SDNN, standard deviation of normal-to-normal RR intervals; RMSSD, root mean square of successive RR interval differences; HF, high frequency; LF, low frequency; HRVB, heart rate variability biofeedback; PTSD, Post-traumatic stress disorder; RCT, randomized controlled trial.

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HRV reflects the ability of the cardiac system to adapt to intrinsic and extrinsic changes (e.g., stress, exercise); while low HRV is an indicator of risk for cardiovascular morbidity and mortality.[8] Cardiac variability results mainly from short-term autonomic regulation by the sympathetic nervous system (SNS) and the vagus nerve of the parasympathetic nervous system (PNS).[9,10] Both of these interdependent systems modulate heart rate (HR) by either accelerating or decelerating it according to physiological mechanisms involved in short-term HRV regulation, especially baroreflex control and respiratory sinus arrhythmia (RSA).[9] The first regulates blood pressure (BP) by increasing HR when BP decreases and vice versa; the second increases HR during inspiration and decreases HR during expiration.[11] Other physiological mechanisms are involved in the long-term regulation of HRV, such as physiological factors (e.g., hormones, inflammation), neuropsychological factors (e.g., emotions, stress, cognitive regulation) and environmental factors or lifestyle (e.g., physical exercise, tobacco, alcohol).[12]

HRV is characterized by time variations between each heartbeat and is linked to the RR interval of the electrocardiogram (ECG).[13] HRV level is measured in the time domain and in the frequency domain of the ECG or pulse wave recordings.[13,14] In the time domain, the standard deviation of normal-to-normal RR intervals (SDNN) reflects both sympathetic and parasympathetic modulations on HR; and the root mean square of successive RR interval differences (RMSSD) reflects predominantly parasympathetic activity.[13,14] In the frequency domain, short-term HRV analysis is mainly based on the HRV power spectrum divided into high frequency (HF; from 0.15 to 0.4 Hz) and low frequency (LF; from 0.04 to 0.15 Hz) bands that tend to correlate with certain physiological mechanisms. HF-band reflects respiratory effects on HR modulation (RSA) mediated by parasympathetic cardiovagal outflow producing rapid changes in HR. Beside, LF-band corresponds to baroreflex activity, a feedback loop between baroreceptors and brainstem that regulates BP by both sympathetic and parasympathetic outflow producing slightly slower changes in HR.[13,14] Specifically, LF-band should be considered as a reflection of the baroreflex function induced by both the sympathetic and parasympathetic HR modulations and not as the only reflection of the sympathetic tone.[15] Interpretation of the HRV power spectrum must therefore take into account the complexity of the physiological mechanisms involved in autonomic cardiovascular adaptations such as RSA and baroreflex activity.

Given neural exchanges between the central autonomic network and cardiac activity, HRV is influenced by the brainstem, cortical and subcortical structures and, reciprocally, cerebral activity could be influenced by HRV.[7,16] Current research indicates that the amygdala, insula and anterior cingulate are involved in emotional processing, which suggests a link between emotional states and HRV.[17,18] Since vagal outflow predominates at rest through powerfull cardiomoderator effects, authors developed a neurovisceral integration model in which vagal activity supports reciprocal interaction between heart and brain, suggesting that HRV could modulate cerebral activity.[19] Thereafter, the psychophysiological model proposed by McCraty and these colleagues have suggested that a specific heart rhythm pattern occurs when HR synchronizes itself with other oscillatory systems, such as RSA and baroreflex at a specific resonance frequency corresponding to ~6 breaths/min. Synchronization of these oscillatory systems is displayed by sine wave oscillations of breathing, HR and BP reflecting a "coherence state". Under these conditions, authors suggested that HRV is largely increased through the augmentation of vagal functioning, which could positively affect brain activity and especially emotional regulation.[20] These heart-brain interactions resulting from vagal efferents and afferents suggest the contribution of vagal nerve activity in the pathophysiological mechanisms of chronic diseases and the possible issues of vagal-activating interventions.[6]

Heart rate variability biofeedback (HRVB) is a non-pharmacological intervention used for its regulatory effects on autonomic cardiac regulation by increasing HRV and restoring cardiac vagal control, and improving emotional self-regulation.[21,22] When breathing approximates 6 breaths/min, baroreflex and breath synchronize themselves producing a specific pattern of HRV signal.[23] This cardiac coherence state occurs at a resonance frequency of approximately 0.1 Hz, creating high amplitudes in sine wave oscillations of the HRV signal and a notable peak in the LF-band of the HRV power spectrum.[24] Since the late 1990s, numerous studies have investigated the effects of HRVB on various psychophysiological symptoms related to chronic diseases,[22,25] and a standardized method of training has been proposed by Lehrer.[26] A meta-analysis has already highlighted the positive effects of HRVB on stress,[27] and a systematic review indicated possible benefits of HRVB on sports performance.[28]

In the current systematic review, we aimed to determine whether HRVB could be a feasible and effective non-pharmacological intervention to manage patients affected by chronic diseases. Consequently, we reviewed all studies involving adult patients that investigated HRVB training effects on psychophysiological outcomes related to chronic diseases.

2. Method

2.1. Search strategy

Articles published up to March 31, 2020 in the electronic databases PubMed/Medline, Springer Link, and ScienceDirect/Elsevier were screened. The search strategy with keywords and filters is presented in Table 1.

2.2. Eligibility criteria

Included in the systematic review were all studies that met the following specific requirements of our predefined PICOS criteria relating to population, intervention, comparison, outcome and study design: scientific research articles in English and French including adult patients (older than 18 years) affected by a chronic disease; reporting the effects of HRVB as an intended treatment for psychophysiological symptoms considered as dependent variables; evaluating training effects of HRVB from at least two sessions with instructions for control frequency breathing at approximately 6 breaths/min; and using a biofeedback device displaying the HRV in real time. To provide a comprehensive

Table 1
Search strategy.

PubMed/ Medline	Springer Link	ScienceDirect/Elsevier
Directly in the search bar ("biofeedback") AND ("heart rate variability" OR "cardiac coherence" OR "psychophysiological coherence" OR "respiratory sinus arrhythmia") AND ("intervention" OR "training") AND ("pain" OR "fatigue" OR "anxiety" OR "depression" OR "quality of life" OR "sleep disturbance" OR "cognitive abilities" OR "executive functioning" OR "inflammation" OR "psychological well-being" OR "emotional distress" OR "hypertension"). Regarding research using ScienceDirect, we used the "research articles" filter and we used ("biofeedback") AND ("heart rate variability" OR "cardiac coherence" OR "psychophysiological coherence" OR "respiratory sinus arrhythmia") AND ("intervention" OR "training")		***Advanced search*** **Find articles with these terms:** ("pain" OR "fatigue" OR "anxiety" OR "depression" OR "quality of life" OR "sleep disturbance" OR "cognitive abilities" OR "executive functioning" OR "inflammation" OR "psychological well-being" OR "emotional distress" OR "hypertension") **Title, abstract or keywords:** (« biofeedback ») AND ("heart rate variability" OR "cardiac coherence" OR "psychophysiological coherence" OR "respiratory sinus arrhythmia") AND ("intervention" OR "training")
No filters	Filters: "Articles"; English and French languages	Filters: "Research articles"

review of HRVB intervention for clinical outcomes, we included all study designs and comparison methods with or without a control group. We included studies that implemented HRVB alone or HRVB associated with standard care or HRVB associated with another non-pharmacological intervention, but only if protocol provided a control group receiving the same standard care or the same non-pharmacological intervention so as to evaluate the added value of the HRVB. We excluded studies that combined HRVB training with another non-pharmacological intervention when protocol did not include a control group that allowed to distinguish the HRVB specific effects because of the possible confounding factors in the interpretation of the findings.

2.3. Study selection and data extraction

Study selection was made by manually screening abstracts and then making adjustments based on each article's content to avoid accidental inclusion and exclusion. Articles were first classified according to whether or not they met PICOS criteria; articles matching our eligibility criteria were then catalogued, specifying details on method, measurements, and results. To avoid risk of selection bias, and accidental inclusion and exclusion, the database was reviewed by all co-authors to correct errors where necessary.

3. Results

Our search strategy yielded a total of 626 articles (PubMed: 95; ScienceDirect: 23; Springer Link: 508), with 3 additional publications identified from sited references. Using the selection process presented in Fig. 1, several records were removed because of redundancy (duplicated: 39) or were not an original research article (protocols, conference proceedings or any publication that did not specify the method and results in detail: 127). On the remaining 463 articles, 434 were excluded by applying the previously detailed eligibility criteria in this order: English or French language; adult patients with chronic disease excluding some clinical situations, such as substance use disorders (considering the complex situation involving behavioral disorders) and pregnant women (not being a chronic disease); interventional study of HRVB training (2 or more sessions with specific breathing instructions); and the use of a biofeedback tool (pulse sensor or ECG) with real-time HRV display. A total of 29 remaining research articles were included, involving 1127 patients with sample size ranged from 10 to 210 and assessing psychophysiological outcomes as a main objective. Among them, 14 were randomized controlled trials, 7 were uncontrolled studies, and the remainder were pilot, feasibility or experimental studies providing wait-list control group, healthy control group, standard care control group or other intervention control group. For uncontrolled studies, only those evaluating the effects of HRVB alone were included. For controlled studies, the intervention and control groups differed only by the HRVB intervention: HRVB VS no intervention; HRVB VS other interventions; HRVB + standard care VS same standard care; HRVB + other intervention VS same other intervention. They are summarized in Table 2 and classified by type of chronic disease.

3.1. Feasibility in chronic patients

3.1.1. Adhesion

HRVB feasibility was tested among patients with various chronic diseases and in a variety of clinical contexts. The maximum dropout rate reported was of almost 25 % for the HRVB participants in a one-year longitudinal study [29] and measured participation rates were over 70 %

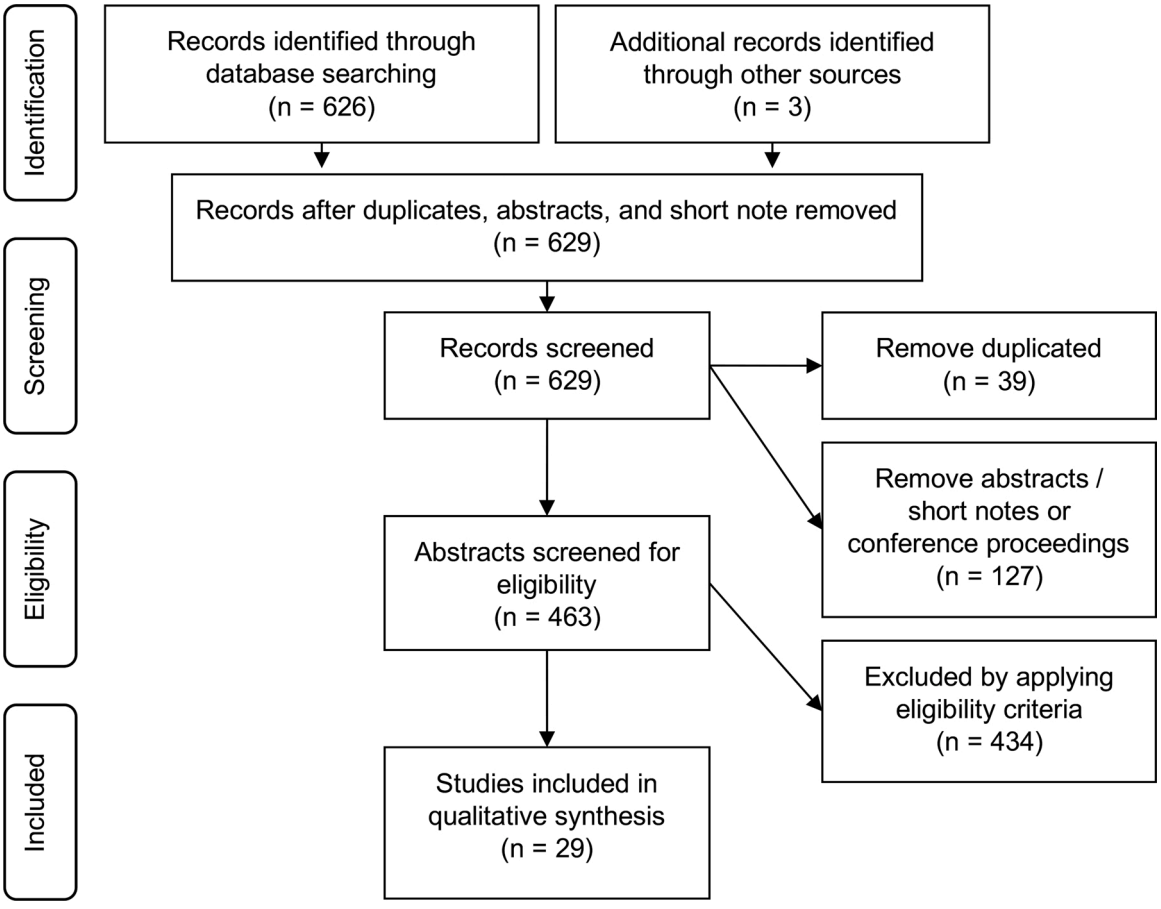

Fig. 1. PRISMA flow diagram.

Table 2
Main features of 29 included studies.

Study	Sample	Design	Dependent variables and assessment time	HRVB intervention	Feasibility	Significant improvements in HRVB group	HRV indices	Non-significant results
Cardiovascular diseases								
Climov et al. (2014)	Coronary artery disease Age = 45–80	• RCT • HRVB + standard care (n = 13) • Standard care (n = 11)	HADS; Type D personality; BP; HRV • Pre-post-intervention	10 sessions (45–60 min) twice a week + daily practice	• 7 dropouts (occupations and time constraint)	No data	• Increase of mean coherence score** correlated with SDNN	• HADS; Type D personality; BP
Nolan et al. (2005)	Coronary heart disease Age = unknown	• RCT • HRVB (n = 27); • Autogenic relaxation + psychotherapy (n = 19)	PSS; CES-D; HRV • Pre-post-intervention	5 sessions (90 min) over 4 weeks	No data	• Stress (PSS**); • Depression (CES-D**)	• Decrease of PSS** and CES-D** associated with increase of HF power* only in HRVB group	• No difference between groups
Nolan et al. (2010; 2012)	Hypertension Age = 35–64	• RCT • HRVB (n = 35) • Autogenic relaxation (n = 30)	BP; baroreflex sensitivity; hsCRP; IL-6; HRV • Pre-post-intervention	6 sessions (60 min) + 20-min daily practice over 8 weeks	No data	• Daytime BP** and 24 h systolic BP*, and pulse pressure*	• Increase of HF power** and IBI** during cognitive task • Increase of hsCRP inversely associated with change in HF power*, baroreflex sensitivity*, and IBI*	• Baroreflex sensitivity • Change in IL-6 not associated with change in HRV indices and baroreflex sensitivity
Patron et al. (2013)	After cardiac surgery Age = 52–69	• RCT • HRVB + stress management (n = 13) • Stress management (n = 13)	STAI; CES-D; HRV • Pre-post-intervention	5 sessions (45 min) over 2 weeks + 15-min daily practice	No data	• Depression (CES-D*)	• Increase of total power**; • Change in HRV inversely associated* with change in depression	• STAI
Swanson et al. (2009)	Heart failure (LVEF ≤ 50 %) Age = 42–70	• RCT • HRVB (n = 21) • quasi-false EEG-BF training (n = 14)	CES-D; LFHQ; PANAS; 6MWT • Pre-post-intervention • 12-week follow-up	6 sessions (45 min) weekly + 20-min daily practice over 6 weeks	• 4 dropouts (financial, transport or medical problems)	• Exercise tolerance (6MWT*) at follow-up	No data	• LFHQ, PANAS, and CES-D
Yu et al. (2018)	Coronary artery disease Age = 35–70	• RCT • HRVB + standard care (n = 105) • Standard care (n = 105)	BDI-II; CHI-SF; HRV; cardiovascular prognosis ▪ Pre-post-intervention ▪ 1-year follow-up	6 sessions weekly	• Dropout rate of 26.47% in the HRVB group and 34.44% in the control group	• Depression (BDI-II total score**; cognitive depression subscale**); • Hostility** (CHI-SF); • Results maintained at follow-up; • Reduction of readmission* and emergency visits** at follow-up	• Decrease of breathing rate**; • Increase of LF power** maintained at follow-up	• No difference between groups at follow-up for reduction of all-cause readmission and all-cause emergency visits
Obesity								
Meyer et al. (2018)	Obese patients (30 < BMI < 45) Age = 18–45	• Pilot study • HRVB (n = 10) • Wait-list control (n = 10)	PSS; PHQ-D; SF-36; ASF; HRV • Pre-post-intervention • 3-months follow-up	6 sessions weekly	• 8 discontinued the intervention	• Depression (PHQ-D*); • Stress (PSS*); • Self-efficacy (ASF sum score*); • Quality of life (mental sum score** maintained at follow-up and physical sum scores* at follow-up on SF-36) • Pooled results	▪ Increase of SDNN**, total power**; ▪ Decrease of breathing rate* maintained at follow-up	No data
Asthma		• RCT			▪ 18 dropouts;			

(*continued on next page*)

Table 2 (*continued*)

Study	Sample	Design	Dependent variables and assessment time	HRVB intervention	Feasibility	Significant improvements in HRVB group	HRV indices	Non-significant results
Lehrer et al. (2004)	Asthma Age = 27−47	• Full protocol: HRVB + specific instructions about breathing (n = 23) • HRVB alone (n = 22) • EEG-BF (n = 24) • Waiting-list control (n = 25)	Asthma symptoms; medication consumption; respiratory resistance; HRV • Pre-post-intervention	10 sessions weekly + 20-min twice daily practice	▪ >70 % participation rate of daily practice	▪ Medication consumption** in two HRVB groups; ▪ Asthma symptoms in full protocol group**, HRVB group*, and EEG-BF group*	▪ Increase of HRV total power** and LF power** in two HRVB groups	▪ No difference between two HRVB groups; ▪ No difference with EEG-BF group for asthma symptoms
Lehrer et al. (2018)	Asthma Age = 27−47	▪ RCT ▪ HRVB group (n = 31) ▪ EEG-BF + relaxing music + paced breathing ~15 breaths/min group (n = 33)	MCT; ACT; AQOL; eNO; daily symptoms and peak flows; spirometry and impulse oscillometry ▪ Pre-post-intervention	*Short protocol* (n = 20): 6 HRVB sessions over 10 weeks + 20-min daily practice *Long protocol* (n = 11): 10 HRVB sessions over 10 weeks + 20-min daily practice	▪ 19 % dropout	• Asthma symptoms (ACT**; AQOL**); • Sensitivity of airways (MCT**); • Pulmonary function (peak flow*); ▪ Episodes of poor asthma control* and airways inflammation (eNO*)	No data	• No difference between groups at post-intervention for ACT, AQOL, MCT, and peak flow; ▪ No difference between short and long protocol
Chronic brain injury								
Kim et al. (2013)	Chronic brain injury Age = 23−63	▪ Pilot study ▪ HRVB (n = 13) ▪ No control group	IVA; CPT; BRIEF-A; HRV ▪ Pre-post-intervention	10 sessions weekly + home practice from session 4	▪ No data	• No data	▪ Increase of coherence ratio* and LF/HF**; ▪ Emotional control and working memory (BRIEF-A) correlated with coherence ratio* and LF/HF**; ▪ Attention (IVA + CPT) correlated with LF/HF**	No data
Chang et al. (2020)	Acute ischemic stroke	▪ RCT ▪ HRVB + standard care (n = 19) ▪ Standard Care (n = 19)	MMSE; HADS; HRV ▪ Pre-post-intervention ▪ 1 and 3 months	4 supervised sessions in 4 days +20 min daily practice over 3 months	▪ 3 dropped out ▪ Supervised sessions carried out on bedside	• Anxiety and depression (HADS*) at 1 and 3 months • Cognitive functions (MMSE**) at 1 and 3 months	▪ Decrease of heart rate* at 1 and 3 months; ▪ Increase of SDNN*, RMSSD*, LF* and total power* at 1 and 3 months	No data
Chronic pain								
		▪ RCT	IBS-SSS; HADS				No data	

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Table 2 (*continued*)

Study	Sample	Design	Dependent variables and assessment time	HRVB intervention	Feasibility	Significant improvements in HRVB group	HRV indices	Non-significant results
Dobbin et al. (2013)	Refractory irritable bowel syndrome Age = 18–60	▪ HRVB (n = 31) ▪ Hypnotherapy (n = 30)	▪ Pre-post-intervention ▪ 3-month follow-up	3 sessions (60 min) +20 min daily practice over 12 weeks	▪ 15 dropouts (7 in HRVB group)	▪ Symptoms (IBS-SSS*) at post-intervention; ▪ Anxiety and depression (HADS*) • Results maintained at follow-up		• No difference between groups for HADS at post-intervention
Hassett et al. (2007)	Fibromyalgia Age = 18–60	▪ Pilot study ▪ HRVB (n = 12) ▪ No control group	MPQ; BDI-II; FIQ; PSQI ▪ Pre-post-intervention ▪ 3-month follow-up	10 sessions weekly + 20-min daily practice	• HRVB was acceptable and easily learned with no adverse effects	• Depression (BDI-II*) maintained at follow-up; • Functioning scores** (FIQ) at follow-up; • Pain (MPQ*) at follow-up	No data	• PSQI
Weeks et al. (2015)	Chronic pain ≥ 3 months (fibromyalgia, headache, neuropathy, …) Age = 45–68	▪ RCT ▪ HRVB (n = 10) ▪ Faded feedback (n = 10): progressive reduction of displaying feedback from 90% to 0%	10-cm visual analog scale (VAS); PDQ; TSK-11 ▪ Pre-post-intervention ▪ 3-month follow-up	9 sessions over 3 weeks	▪ 6 discontinued the intervention; ▪ 3 missed at the follow-up assessment	• No data	No data	▪ Pain intensity on VAS, TSK-11, PDQ
Cancer								
Greenberg et al. (2015)	Non-small cell lung cancer (NSCLC) Age = 46–71	▪ Feasibility study ▪ HRVB group (n = 16) ▪ No control group	HADS; PHQ-8; FACT-L; Distress Thermometer and Problem Areas ▪ Pre-post-intervention	6 sessions (30–45 min) during chemotherapy + 20-min daily practice	▪ 8 patients included; ▪ 1 completed the protocol; ▪ HRVB done during chemotherapy; ▪ Ability to reduce respiration rate, decrease of heart rate and stress across training sessions	• *No statistical analyses*	No data	No data
Depression								
Caldwell et al. (2018)	Major depressive disorder Age = 18–25	▪ RCT ▪ HRVB + psychotherapy (n = 10) ▪ Psychotherapy (n = 10) ▪ Non-depressed control group (n = 11)	BDI-II; HRV ▪ Pre-post-intervention	5 sessions + 15–20 min home-practice 4–5 times per week over 6 weeks	No data	▪ Depression (BDI-II**)	▪ SDNN**	No data
Hartogs et al. (2017)	Major depressive disorder Age = 23–62	▪ Experimental study ▪ HRVB (n = 10) ▪ No control group	BDI-II; POL; HRV ▪ Pre-post-intervention	8 sessions (45–60 min) weekly + 20-min daily practice	▪ 3 dropouts (lack of motivation); ▪ 7 completed the full protocol; ▪ 1 deterioration in depression	Clinical improvements in 5 patients: ▪ Depression (BDI) ▪ Resilience (POL-Autonomy scores)	▪ Increase of coherence score during protocol for 5 patients	No data
Karavidas et al. (2007)	Major Depressive Disorder Age = 25–58	▪ Experimental study ▪ HRVB (n = 11) ▪ No control group	HAM-D; BDI-II; HRV ▪ Pre-post-intervention	10 sessions (60 min) weekly + 20-min twice daily practice	▪ 3 dropouts; ▪ 8 completed the protocol	▪ Depression (BDI-II total score**, cognitive**, and neurovegetative**	▪ Increase of SDNN**, pNN50**, LF power**;	No data

(*continued on next page*)

Table 2 (*continued*)

Study	Sample	Design	Dependent variables and assessment time	HRVB intervention	Feasibility	Significant improvements in HRVB group	HRV indices	Non-significant results
						components; HAM-D total score**)	■ Decrease of mean HR*	
Lin et al. (2019)	Major depressive disorder Age = 20–75	■ Case-control study ■ HRVB (n = 24); ■ Wait-list control (n = 24)	BAI; BDI-II; PSQI; PSAS; HRV ■ Pre-post-intervention ■ 1-month follow-up	6 sessions (60-min) weekly + 10-min daily practice	■ 5 dropouts	■ Depression (BDI-II total score**, cognitive depression*, somatic depression*); ■ Anxiety (BAI total score**); ■ Sleep (PSAS total score*, PSQI total score**, and cognitive arousal of PSAS**) ■ Results maintained at follow-up	■ Decrease of breathing rate**; ■ Increase of SDNN**, LF power*, LF/HF*, total power**; ■ Results maintained at follow-up	■ No difference between groups for PSQI and PSAS total scores
Siepmann et al. (2008)	Depression Age = 18–47	■ Pilot study ■ HRVB (n = 14) ■ Healthy control group	STAI; BDI ■ Pre-post-intervention ■ 2-week follow-up	6 sessions (25 min) over 2 weeks	No data	■ Anxiety (STAI*); ■ Depression (BDI scores*) ■ Results maintained at follow-up	■ Decrease of heart rate** maintained at follow-up	No data
Chronic stress								
De Bruin et al. (2016)	Chronic stress evaluated from PSS score Age = 18–40	■ RCT ■ HRVB (n = 25) ■ Mindfulness meditation (n = 27) ■ Physical exercise (n = 23)	ACS; BRIEF-A; FFMQ-SF; SCS-SF; PSWQ ■ Pre-post-intervention ■ 6-week follow-up	Over 5 weeks: 1st week = 10 min/day 2nd week =15 min/day 3rd to 5nd week = 20 min/day	■ 19 dropouts, 1 in the HRVB group (occupations and time constraint); ■ Greater improvements in patients >70% participation rate	■ Attention control* (ACS); ■ Executive functioning* (BRIEF-A); ■ Mindful awareness* (FFMQ-SF); ■ Self-compassion* (SCS-SF); ■ Worrying* (PSWQ) ■ Little effect sizes at follow-up for attention control and executive functioning compared to other groups	No data	■ No difference between groups at post-intervention and follow-up
Hallman et al. (2011)	Stress related chronic neck-shoulder pain Age = 25–50	■ Pilot study ■ HRVB (n = 12) ■ Control group took part in session 1 and 10 without instructions in between (n = 12)	Borg CR10; SMSS; HADS; SF-36; NDI; HRV ■ Pre-post-intervention	10 sessions weekly	■ No data	■ Quality of life (Bodily pain*, social function*, and vitality** on SF-36)	■ Increase of LF power**; Increase in LF power*, pNN50*, and IBI*during recovery from stress	■ SMSS, Borg CR10, and NDI, HADS
Van der Zwan et al. (2015)	Chronic stress evaluated from PSS score Age = 18–40	■ RCT ■ HRVB (n = 26) ■ Physical exercise (n = 23) ■ Mindfulness meditation (n = 27)	DASS; PSQI; SPW ■ Pre-post-intervention ■ 6-week follow-up	Over 5 weeks: 1st week = 10 min/day 2nd week =15 min/day 3rd to 5nd	■ 9 missed post-test and/or follow-up assessments; ■ Greater improvements in patients >70 %	■ Stress**, anxiety**, and depression** (DASS); ■ Well-being** (SPW); ■ Sleep quality* (PSQI);	No data	■ No difference between groups at post-intervention and follow-up

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Table 2 (*continued*)

Study	Sample	Design	Dependent variables and assessment time	HRVB intervention	Feasibility	Significant improvements in HRVB group	HRV indices	Non-significant results
				week = 20 min/ day	participation rate	▪ Results maintained at follow-up		
Psychiatric disorders								
Jester et al. (2018)	Psychiatrics symptoms (depressive, anxiety, and bipolar disorders) Age = 63−96	▪ Experimental study ▪ HRVB (n = 20) ▪ No control group	STAI; BDI-II; TMT-A-B ▪ Pre-post-intervention	6 sessions (30 min) over 3 weeks + home practice twice weekly	▪ Positive effects of HRVB on anxiety or worry (67 %), on depression or sadness (56 %), on stress (44 %); or no effects of HRVB on stress (50 %) reported by patients; ▪ Slight negative effects on anxiety (competitive nature of BF software) reported by 1 patient	▪ Depression** (BDI-II); ▪ State anxiety**, and trait anxiety** (STAI); ▪ Attention skills (TMT-A**)	No data	No data
Ginsberg et al. (2010)	Post-traumatic Stress Disorder Age = 27−37	▪ Pilot study ▪ HRVB (n = 5) ▪ Healthy control group	ATTN/IM; HRV ▪ Pre-post-intervention	4 sessions weekly + daily practice over 4 weeks	• No data	▪ Cognitive capacities with list learning total variable** (ATTN/IM)	▪ Increase of coherence ratio** and LF power*; Change in cognitive performance correlated with change in coherence ratio**	No data
Schuman et al. (2018)	Post-traumatic Stress Disorder Age = 26−50	▪ Pilot Study ▪ HRVB (n = 6) ▪ Waiting-list control with diaphragmatic breathing (n = 6)	PCL-5; HRV ▪ Pre-post-intervention ▪ 4-week and 16-week follow-up	1 session + 10−15 min twice daily practice over 4 weeks	• 10 completed the protocol; • >70 % participation rate of daily practice; • Symptoms reduction of anger, anxiety, and sleep disturbance experienced by patients	▪ PTSD-specific symptoms (PCL-5*) maintained at follows-up ▪ Pooled results	▪ Increase of RMSSD* at 16-week follow-up	No data
Tan et al. (2011)	Post-Traumatic Stress Disorder Age = 24−62	▪ Pilot study ▪ HRVB + standard care (n = 10) ▪ Standard care (n = 10)	CAPS; PCL-S ▪ Pre-post-intervention	8 sessions (30 min) + 20-min twice daily practice over 8 weeks	• 1 dropout (transport problem); • HRVB intervention evaluated as 8/10 by patients for satisfaction who reported good experience.	▪ PTSD-specific symptoms (CAPS**; PCL-S*)	No data	▪ No difference between groups at post-intervention
Trousselard et al. (2016)	Remitted schizophrenia Age = 25−46	▪ Pilot study ▪ HRVB (n = 10) ▪ No control group	STAI; DSP; PANSS; WEMWBS; FMI ▪ Pre-post-intervention	8–12 sessions (60 min) weekly + daily relaxation exercises	• No dropout; • Mostly would to continue after cessation; ▪ More improvements in patients with high level of symptoms	▪ Mindfulness* (FMI); ▪ Anxiety stressors* and emotional stressor* (DSP)	No data	WEMWBS, PANSS, STAI
Zucker et al. (2009)		▪ Pilot study ▪ HRVB (n = 19)	PTS-T; PCL-C; BDI-II; ISI; HRV		• Ability to increase HRV amplitude	▪ Depression (BDI-II*);	▪ Increase of SDNN*;	▪ No difference between

(*continued on next page*)

Table 2 (*continued*)

Study	Sample	Design	Dependent variables and assessment time	HRVB intervention	Feasibility	Significant improvements in HRVB group	HRV indices	Non-significant results
	Post-Traumatic Stress Disorder Age = 18–60	■ Progressive muscle relaxation (n = 19)	■ Pre-post-intervention	20-min daily practice over 4 weeks		■ PTSD-specific symptoms (PTS-T**; PCL-C**); ■ Sleep (ISI score*)	Change in SDNN associated with change in PCL-C* and BDI* scores	groups at post-intervention for PST-T, PCL-C, and ISI

*<0.05; **≤0.01; "No data" indicates that article did not mentioned this information.
6MWT: 6 min walk test; **ACS:** attention control scale; **ACT:** asthma control test; **AQOL:** asthma quality of life; **ASF:** self-efficacy; **ATTN/IM:** test battery was modeled on Vasterling's studies; **BAI:** Beck anxiety inventory; **BDI-II:** Beck depression inventory; **BP:** blood pressure; **BRIEF-A:** behavior rating inventory of executive function-adult; **CAPS:** clinician-administered PTSD scale; **CES-D:** center for epidemiological studies-depression scale; **CHI-SF:** Chinese hostility inventory-short form; **CPT:** Continuous Performance Test; **DASS:** depression anxiety stress scales; **DSP:** derogatis stress profile; **EEG-BF:** electroencephalogram biofeedback; **eNO:** exhaled nitric oxide; **FACT-L:** functional assessment of cancer therapy-lung; **FFMQ-SF:** five facet mindfulness questionnaire-short form; **FIQ:** fibromyalgia impact questionnaire; **FMI:** Freiburg mindfulness inventory; **HADS:** hospital anxiety and depression scale; **HAM-D:** Hamilton depression scale; **hsCRP:** high-sensitivity C-reactive protein; **IBI:** interbeat interval; **IBS-SSS:** Irritable Bowel Syndrome Symptom Severity Scores; **IL-6:** interleukin-6; **ISI:** insomnia severity index; **IVA:** integrated visual and auditory; **LFHQ:** living with congestive heart failure questionnaire; **LVEF:** left ventricular ejection fraction; **MCT:** metacholine challenge test; **MMSE:** mini-mental status examination; **MPQ:** McGill pain questionnaire; **NDI:** neck disability index; **PANAS:** positive and negative affect scale; **PANSS:** positive and negative syndrome scale; **PCL-5:** PTSD checklist for the DSM-5; **PCL-C:** PTSD checklist- civilian version; **PCL-S:** PTSD checklist-specific; **PDQ:** pain disability questionnaire; **PHQ-8:** patient health questionnaire; **PHQ-D:** patient health questionnaire-depression and anxiety; **POL:** positive outcome list; **PSAS:** pre-sleep arousal scale; **PSQI:** Pittsburgh sleep quality index; **PSS:** perceived stress scale; **PSWQ:** Penn State Worry Questionnaire; **PTS-T scale:** PTSD-specific symptoms; **SCS-SF:** self-compassion scale-short form; **SF-36:** short form general health survey; **SMSS:** stress medicine symptom scale; **SPW:** scales of psychological well-being; **STAI:** Spielberger state anxiety inventory; **TMT-A-B:** trail making test part A and B; **TSK-11:** 11-item tampa scale of kinesiophobia; **WEMWBS:** Warwick–Edinburgh mental well-being scale.

for HRVB daily practice.[30,31] Studies that reported reasons for dropouts included the following explanations: time constraints, transport issues,[32–35] lack of motivation,[36] financial issues [34] and medical problems.[34,37] One protocol was terminated prematurely because of high dropout in lung cancer patients due to disease-related physical health deterioration or death (therefore, unrelated to the HRVB protocol per se).[37]

3.1.2. Satisfaction

Overall, patients reported satisfaction in stress reduction and positive emotion enhancement during biofeedback and maintained long-term persistent benefits.[31,35,38,39] Out of all the studies reviewed, none of the participants reported dissatisfaction. Patients in remitted schizophrenia willingly completed the intervention with no attendance obligation and most wished to continue thereafter because of reported feelings of psychological benefits.[39] Among older patients with psychiatric symptoms, a 67 % satisfaction rate was reported for positive effects on anxiety or worry, along with a 56 % satisfaction rate for depressive state or sadness and 50 % satisfaction regarding stress.[38]

3.1.3. Adverse effects

No serious adverse effects were related to HRVB practice, which confirms the feasibility of HRVB in chronic patients. Some slight adverse effects were reported such as anxiety because of the inherent pressure felt by patients to meet the specified breathing targets of the biofeedback device.[38] To avoid possible aggravations related to slow breathing and hyperventilation, a familiarization period was implemented in a protocol to progressively decrease the respiration rate from a natural rhythm of ~14 breaths/min to a target rate of ~6 breaths/min.[29,40]

3.2. Effectiveness on psychophysiological outcomes

3.2.1. Hypertension and cardiovascular diseases

A randomized controlled trial (RCT) totalizing 65 patients examined BP as a primary objective and concluded that HRVB was effective in reducing 24-h systolic BP (-2.1 ± 0.9 mmHg, $p = 0.03$) and 24-h pulse pressure (-1.4±0.6 mmHg, $p = 0.02$) after 8 weeks of daily practice and no change was observed for controls (autogenic relaxation).[41] A recent longitudinal RCT of 210 patients with coronary artery disease indicated an improvement of one-year cardiovascular prognosis, demonstrated by a reduction in readmission and all-cause emergency visits compared to controls.[29] In contrast, a study including 24 patients with coronary artery disease did not find a reduction in BP.[32] In the latter case, all baseline systolic and diastolic BP values were within normal limits because the patients were already on beta-blocker medication at the start of the study, which represents a significant limitation of the findings. As a result, HRVB seems to positively affect BP in hypertensive subjects and cardiovascular prognosis in cardiac patients.

3.2.2. Inflammatory state

An inverse association between changes in the inflammatory state (measured from high sensitivity C-reactive protein and interleukin-6) and efferent vagal activity (measured from HF power, RR interval and baroreflex activity) has been observed in a study of 65 hypertensive patients.[42] Authors assumed that an increase in efferent vagal activity could suppress pro-inflammatory factors suggesting possible anti-inflammatory effects of HRVB. These findings are supported by the cholinergic anti-inflammatory reflex model described by Tracey (2007) according to which the efferent neural signaling of vagus nerve mediated by the cholinergic pathway could inhibit cytokine release and prevent inflammatory syndromes.[43]

3.2.3. Asthma disorders

Two RCTs including 94 and 64 patients concluded that both asthma symptoms and pulmonary function improved, and airway inflammation and medication consumption was reduced after 10 weeks of HRVB daily

practice compared to controls, suggesting the high potential of HRVB in the specific management of asthma symptoms.[30,44] HRVB was more effective than electroencephalogram (EEG) biofeedback and standard care in reducing medication consumption [30] and airway inflammation,[44] and it was equally effective as active controls in improving asthma symptoms,[30,44] sensitivity of airways [44] and pulmonary function.[44]

3.2.4. Depression, anxiety and emotional state

Out of 15 studies investigating depression as a dependent variable, 12 reported significant positive effects of HRVB; likewise, in 12 studies examining stress and anxiety, 9 showed significant positive effects of HRVB. Depression, stress and anxiety were significantly reduced in 12 studies totaling 326 various patient profiles who suffered from depression,[36,45–48] chronic pain,[49,50] chronic stress,[51] psychiatric disorders [38,39] and obesity.[52] A reduction in both anxiety and depression was maintained several weeks to 1 year after HRVB training.[29,47–51]

Other positive outcomes related to emotional state were evaluated such as increased mindful awareness, self-compassion or well-being. A decrease in worry or hostility was reported in 2 studies totaling 151 patients affected by chronic stress [33,51] and 1 study of 10 patients in remitted schizophrenia.[39]

3.2.5. Sleep disturbances

Of 4 studies that investigated sleep disturbances, 3 (totaling 162 participants) showed improvements in sleep quality after HRVB in patients with major depressive disorders,[47] post-traumatic stress disorder (PTSD) [53] and anxiety disorders. [51] Improvements in sleep co-occurred with decreases in depression,[47,53] PTSD-specific symptoms [53] and anxiety.[51,54] However, no sleep improvements were measured in 12 fibromyalgia patients despite significant improvement on the other outcomes as depression, pain, and overall functioning.[49]

3.2.6. Specific symptoms of post-traumatic stress disorder

PTSD-specific symptoms reduced significantly after 4–8 weeks of HRVB training in 3 studies including 60 patients.[31,35,53] Results showed long-term effects at the 16-week follow-up [31] and were associated with reductions in insomnia and depression.[53] HRVB failed to be more effective than standard care in a study with a small sample size of 20 patients [35] and seemed to have equal effects as progressive muscle relaxation in another study involving 38 participants.[53]

3.2.7. Cognitive performances

Improvements in cognitive abilities have been reported with significant increases of attention skills and executive functioning in patients affected by chronic stress,[33] attention skills in patients with psychiatric symptoms,[38] and memory in PTSD patients.[55] Additionally, 38 patients with acute ischemic stroke showed significant improvements of cognitive function.[40] However, in 13 patients with chronic brain injury, no enhancement of cognitive skills was found, probably due to the nature of neurological damage.[56]

3.2.8. Pain

After HRVB training, refractory pain symptoms were reduced in 3 studies involving 12 fibromyalgia patients,[49] 61 patients with irritable bowel syndrome [50] and 24 patients with stress-related chronic neck-shoulder pain.[57] Two studies revealed that benefits were maintained 3 months after the HRVB training.[49,50] However, these results are nuanced by another study that did not show significant pain reduction in patients with various profiles of chronic pain.[58] No data was provided regarding the prescription and/or consumption of painkillers.

3.2.9. Lifestyle

Improvements in quality of life, especially a more active lifestyle and an increase in both social and physical functioning, co-occurred with a decrease of pain [50,57] and PTSD-specific symptoms.[31,53] In fibromyalgia patients, depressive symptoms decreased at post-intervention, and both quality of life enhancement and pain reduction were reported after 3 months.[49] However, whereas a study of 35 heart failure patients showed exercise tolerance improvements through greater distance covered in 6-min and less dyspnea at the 12-week follow-up, it did not observe significant improvements in quality of life.[34]

4. Discussion

4.1. Changes in HRV could mediate the effects of intervention

Among 31 studies of the systematic review, 18 reported the HRVB effects on HRV. The increased coherence ratio across sessions,[32,36,55,56] indicating high synchronization between respiratory and cardiovascular systems, and the decreased mean HR [41,46,48] and respiratory rate at rest [47,52] across sessions, suggests that patients correctly performed HRVB exercises and illustrate the effects related to regular practice. The HRV indices increasing in the time domain such as SDNN,[40,45–47,52,53] pNN50 [46] or RMSSD,[40] and in the frequency domain such as total power,[30,40,47,52,59] revealed an enhancement of cardiac autonomic control.[13] Several studies demonstrated that improved clinical outcomes were correlated with increased HRV indices. The increased coherence ratio was associated with improved emotional status and cognitive abilities in patients with chronic brain injury [56] and PTSD.[55] The increased total HRV power and the increased SDNN were respectively associated with improved depression scores in patients after cardiac surgery [59] and PTSD patients.[53] The increased HF power was associated with improved stress and depression scores in patients with coronary heart disease [60] and decreased inflammatory status in hypertensive patients.[42] As a result, authors conclude that HRVB may have regulatory effects on the autonomic function involved in physiological systems control by increasing overall HRV and overstimulating cardiac vagus nerve traffic. In this way, the central-autonomic integration of vagal afferents could contribute to better psychophysiological functioning in a more coherent and efficient system.[20] Moreover, 0.1 Hz oscillations as a resonance frequency could play a major role in physical and mental health via optimizing and facilitating interconnected biological process.[61] By enhancing vagal cardiac activity, HRVB could represent a promising method for the management of a wide range of chronic diseases and their symptoms.[22]

4.2. Problematic interpretation of HRV

During spontaneous breathing at rest (approximately 10−15 breaths/min), the HF power reflects PNS arousal and the LF power mainly reflects baroreflex activity modulated by both SNS and PNS.[9] While an increase in HF power undoubtedly demonstrates an increase of PNS arousal, an increase in LF power could indicate an increase of baroreflex control mediated by ANS regulation and cannot unambiguously distinguish sympathetic from parasympathetic contributions. In the studies included in this review, results concerning HRV in the frequency domain were overall interpreted as the reestablishment of cardiac vagal control, represented in either HF or LF bands. Indeed, the influence of respiratory rate on HRV frequency spectrum reveals that vagal activity may cross over into the LF-band for a respiratory rate below 9 breaths/min.[7,14,16] This HRV power spectrum interpretation is supported by recent results showing that HRV power in the LF-band could be eliminated by parasympathetic blockade under slow paced breathing condition in healthy subjects, demonstrating the contribution of cardiac vagal activation over a low frequency range of 4–9 breaths/min.[62] In this context, some researchers suggest to reconsider the frequency limit between HF and LF-bands currently at 0.15 Hz by shifting it at 0.1 Hz in order to consider the specific effects of slow paced breathing on the HRV power spectrum and the complex interplay between PNS and SNS signaling heart-brain interactions. [61]

Several methodological aspects regarding HRV signal acquisition differed between protocols, such as recording duration, device used

(ECG or pulse sensor), HRV parameters measured and conditions of breathing. Breathing was never monitored in any of the protocols, and therefore no information about frequency breathing, tidal volume or inspiration to expiration ratio was provided despite their known effects on HRV.[63] Since changes in breathing patterns could influence the HRV power spectrum as a confounding factor, it is recommended that breathing parameters be monitored to interpret the results more accurately.[16] Additionally, other confounders that could be involved in HRV modulation, such as medication and physical activity,[12] must be considered. Consequently, results regarding the HRV indices improvement should be carefully interpreted as they do not demonstrate a direct cause-and-effect relationship between HRVB and ANS regulation.

4.3. HRVB versus other interventions

As part of this systematic review, we also considered the various protocol designs. HRVB was generally effective compared to standard care or wait list control groups [29,30,45,47,52,57] but failed to be more effective than active controls involving other non-pharmacological interventions.[30,33,44,50,51,53,60] This is not surprising given that autogenic relaxation,[60] progressive muscle relaxation,[53] electroencephalogram biofeedback,[30,44] hypnotherapy,[50] mindfulness meditation and physical exercise [33,51] have positive effects on psychophysiological outcomes. None of the other non-pharmacological interventions used as a control condition improved HRV indices, confirming the specific effects of HRVB on autonomic cardiac regulation (Table 2). When HRVB is associated with standard care,[45] results support the feasibility of HRVB as an adjunctive treatment for clinical patients. However, by choosing only HRVB training without other non-pharmacological intervention because of possible confounding factors, we excluded some of the studies that offer interesting prospects of combined programs of non-pharmacological interventions in chronic disease management, such as physical exercise,[64] health education,[65] or muscle relaxation.[66]

4.4. Recommendations related to HRVB training schedules

Most reviewed protocols offered 4–12 supervised sessions supported by regular home practice. Supervised sessions were provided to ensure the achievement of HRVB exercises, while home practice was intended to reinforce diaphragmatic breathing instruction and to stimulate HRV reactivity. Authors noted a dose-response effect between HRVB practice and symptomatology reduction,[33,51] suggesting the importance of a regular practice and the existence of a practice threshold at which HRVB could produce the expected effects. Based on the reviewed articles, we can assume that optimal practice should include at least one supervised session followed by regular home practice of at least 10 min daily for 4 weeks. This conclusion is similar to previously published guidelines for HRVB protocols recommending 5 supervised sessions with 20-min daily practices.[26] Considering dropouts due to time constraints, shorter practice times might be preferred by patients. However, HRVB practice is likely effective when specifically adapted to the patient profile according to their abilities, with the possibility of offering more supervised sessions and longer protocols when necessary.

4.5. Recommendations related to HRVB training content

A variety of recommendations have been made by authors of the reviewed protocols: include a familiarization period of slow breathing practices at the beginning of the protocol to avoid slight adverse effects (anxiety or breathlessness) [29,40]; introduce pursed-lips abdominal breathing with slightly prolonged exhalation to learn the slow abdominal breathing technique [30,40]; and progressively reduce the time exposed to visual biofeedback throughout the training to promote greater autonomy in HRVB practice.[58] Lehrer's protocol warns against breathing too deeply to overcompensate for slow breathing [26] and a brief anti-hyperventilation instruction (*"In order to avoid hyperventilation during the paced breathing task, please avoid excessively deep breathing. Breathe shallowly and naturally"*) should be provided for individuals naïve to 0.1 Hz breathing.[67] HRVB was often based on approximately 6 breaths/min although it has been established that the individual's HR resonance frequency makes it easier to reach cardiac coherence state.[24] Regarding the inhalation/exhalation ratio (i/e), it seems that a lower i/e ratio produced increased relaxation, stress reduction, mindfulness and positive energy in participants,[68] and specifically a 1/2 ratio could increase baroreflex sensitivity.[69] However, this postulate is discussed by others results showing that a 1/1 ratio is more effective than prolonged exhalation (40 % inhalation and 60 % exhalation) to increase HRV.[70] Therefore, further research is needed to clarify these different points and determine the most effective breathing protocol.

4.6. Perspective for future research

Our results are congruent with other reviews which report positive effects of HRVB on clinical outcomes and conclude that HRVB is feasible and promising to manage patients affected by chronic diseases.[22,25,27] Overall, the authors argued that HRVB could restore autonomic cardiac regulation and emotional self-regulation, which is illustrated by the positive correlation between clinical outcomes and HRV indices.[42,55,56,59,60] Considering the implication of the ANS on pathogenesis [6] and that HRV is a marker of cardiovascular morbidity,[8] a possible regulatory effect of HRVB on autonomic function offers promising prospects for complementary medicine. Although our work presents a qualitative synthesis of HRVB effects and protocols, it is limited by the lack of risk-of-bias assessment of the included studies. Given the heterogeneity of protocols used in HRVB research, future publications should place importance on assessing risk of bias to evaluate for each study its relevance to the findings and carry out meta-analyses to obtain more solid conclusions on the specific effects of HRVB.

Additional RCTs must be conducted to more accurately evaluate the effectiveness of HRVB compared to standard care and active control conditions (e.g., relaxation, mindfulness meditation, physical exercise). Among others, breathing pattern (frequency, tidal volume and inspiration to expiration ratio), physical exercise and medication should be monitored as confounding variables.[12] The different time and frequency indices of HRV must be carefully interpreted according to breathing rate and HRV signal acquisition.[14] An elegant study may inspire researchers for which results were published after inclusion period of the systematic review.[71] It was conducted in depressive patients and protocol was based on a very comprehensive treatment including 5-week of HRVB intervention during inpatient psychiatric rehabilitation. Results showed an increase of both HRV-LF power and coherence ratio, and a decrease of both depression scores and resting breathing rate suggesting promising prospects for clinicians. For a better assessment of autonomic function using HRV, research on alternative analytical methods to improve the extraction of information contained in HRV should be developed and used in the future. Quantitative assessments could also better highlight the effects of HRVB on autonomic cardiac regulation.[72] Finally, with regards to both intervention methods and data reporting, standard guidelines should be followed in future studies to strengthen the impact of meta-analyses and systematic reviews.[16]

5. Conclusion

This systematic review highlights the feasibility of HRVB as an adjunctive treatment in chronic patients. The large heterogeneity in populations and outcomes makes it difficult to draw mechanistic conclusions linking HRVB to intervention results. Our analysis suggests a possible regulatory effect of HRVB on autonomic cardiac regulation by increasing HRV and restoring vagal functioning. The increased vagal traffic could then affect brain activity and improve emotional self-regulation, supporting the utility of HRVB as complementary treatment for a wide range of chronic diseases. Given the reported positive

effects of HRVB on psychophysiological outcomes in various patient profiles, it is clear that HRVB offers promising prospects in chronic diseases management. Further investigations are required to confirm these results, clarify the interpretation of the HRV power spectrum and determine the most effective method in chronic disease management.

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Authors' contributions

CF, FC, GD, TC, QC, CV make substantial contributions to the conception and design of the study. CF conducted the review and CV checked the search strategy and results. All authors contributed to write the manuscript, they have read and approved the manuscript.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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